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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/733,640	12/08/2000	Anthony J. McHugh	ILL03-027-US	2399

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EXAMINER	
GOLLAMUDI, SHARMILA S	

ART UNIT	PAPER NUMBER
1616	

DATE MAILED: 10/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/733,640	MCHUGH ET AL.	
	Examiner	Art Unit	
	Sharmila S. Gollamudi	1616	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *7/26/04*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19,34,38 and 48-59* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-19,34,38 and 48-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Applicant's request for reconsideration of the finality of the rejection of the last Office action is persuasive and, therefore, the finality of that action is withdrawn. Claims **1-19, 34, 38, and 48-59** are pending in this application.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claims 1-6, 34, 38, 48-52, and 58-59 are rejected under 35 U.S.C. 102(a) as being anticipated by WO 00/57852 to Dang et al.

Dang et al disclose injectable compositions and methods for treating solid tumors. Dang et al disclose a formulation comprising a poly(phosphoester) biodegradable polymer and an antineoplastic agent. See abstract. The poly(phosphoester) I is represented by the structure on page 20, which is defined by applicant as a "crystallizable polymer". The biocompatible solvents (N-methyl pyrrolidone) are utilized for ease of synthesis, purification, and handling of the polymer. See page 26, lines 6-10. Dang also discloses the polymer composition containing a blend of polymers, which provides greater flexibility in designing the precise release profile. The additional biocompatible polymers include polyesters, polylactides, polyethylene glycol, polyvinylpyrrolidone, etc. see page 38-39. The polymer composition is in the form of a solid rigid article, a flexible article, or a flowable material wherein over time and at body temperature, the composition assumes the shape of the space it is contained. See page 40. .

Example 4 discloses an aqueous solution of 0.5% polyvinyl alcohol (amorphous polymer) wherein the solution contains 1.37g PVA and 270ml deionized water (emulsifying agent as defined the specification on page 10). The copolymer of example 1 (crystallizable polymer) and lidocaine are mixed together. The polymer/drug combination is then added dropwise to the PVA solution to obtain lidocaine microspheres. Example 6 discloses the use of the amorphous polymer PVA and the crystallizable polymer poly (L-lactide-co-ethyl-phosphate).

Note that the limitation of claim 59 must be inherent since the prior art and the instant claims recite the same structure with the same components unless they are due to conditions that are not recited in the claims. If the latter is the case, then the applicant must include the conditions which provides the limitation.

Claims 1-2, 5-7, 17-18, 34, 38, 48, 51, 52-53, 55-56, and 58-59 are rejected under 35 U.S.C. 102(b) as being anticipated by US patent 5,525,646 to Lundgren et al.

Lundgren discloses a bioresorbable material and an article of manufacture made of such material for medical use to be implanted into a living organism. See column 1, lines 5-10. Lundgren et al disclose the need for implant articles to have both dimension stability (mechanical strength) to retain the shape of the implant during the healing process and malleability so that the material can take the shape of the location it is contained within. See column 1, lines 15-50. Therefore, Lundgren et al disclose a bioresorbable material that comprises at least one amorphous polymer or copolymer selected from the group consisting of poly-d,l-lactide, and copolymers of poly-d,l-lactide and polycaprolactone, poly-l-lactide, or polytrimethylene and

at least one crystalline polymer selected from the group consisting of poly-l-lactide, polycaprolactone and polydioxanone; and a plasticizer (solvent). The composition is a vehicle for the delivery of active agents. See column 5, lines 40-50.

Note that the limitation of claim 59 must be inherent since the prior art and the instant claims recite the same structure with the same components unless they are due to conditions that are not recited in the claims. If the latter is the case, then the applicant must include the conditions which provides the limitation.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1-3, 5, 34, 38, 48-49, 51, and 58-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shukla (6,432,438) in view of WO 88/07366 to Bateman et al.

Shukla teaches a biodegradable vehicle containing a drug, at least two plasticizers (solvent) selected from NMP, PEG, triacetin, etc, and at least one biodegradable polymer, which

is injected into an organism. See abstract. The polymers may be selected from polyesters, polyorthoesters, polyanhydrides, polyaminoacids, pseudopolyamino acids, polyamides, polyalkylcyanoacrylates, and polyphosphazenes. A mixture of polymers may be used to tailor either the release characteristics of BAS in the biodegradable delivery system, or the degradation characteristics of the biodegradable delivery system or both. See column 5, lines 55-67. The reference teaches the blending of two different biodegradable polymers with varying crystallinity and amorphous states to tailor release characteristics of the delivery system. See column 4, lines 25-35.column 9, lines 30-35, and examples. The method of mixing the polymer, solvent, and drug are taught in examples. Note that NMP has a miscibility of a miscibility in water of 7% or less as defined by instant specification.

Although, Shukla teaches the blending of polymers according to their properties to manipulate release rate, Shukla et al do not exemplify the use of a polymer blend consisting of an amorphous polymer and crystalline polymer.

Bateman et al disclose a tablet composition containing a crystalline polymer and an amorphous polymer. See abstract. Bateman et al teach partially crystalline polymers provide for an immediate release whereas amorphous polymers provide for a prolonged release. See page 7, lines 25-35. Further, Bateman teaches that blending crystalline and amorphous polymers in carious ratios, a range of active release can be provided. See page 8, lines 1-6.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Shukla et al and Bateman et al and utilize a polymer blend of an amorphous polymer and an crystalline polymer. One would have been motivated to do so since Bateman teaches that amorphous polymers tend to provide a sustained release whereas

crystalline polymers provide a immediate release and by varying the ratio of both types of polymer, the desired release rate can be obtained. Therefore, one would have been motivated to look to Bateman's specific teaching that the instant polymer blend provides for the desired release rate and apply it to Shukla's broad teaching that varying the properties, such as crystallinity and amorphous states, of the biodegradable polymers tailors the release rate of the delivery device.

Claims 1-3, 5, 34, 38, 48-49, 51, and 58-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over Shukla (6,432,438) in view of US patent 5,525,646 to Lundgren et al.

Shukla teaches a biodegradable vehicle containing a drug, at least two plasticizers (solvent) selected from NMP, PEG, triacetin, etc, and at least one biodegradable polymer, which is injected into an organism. See abstract. The polymers may be selected from polyesters, polyorthoesters, polyanhydrides, polyaminoacids, pseudopolyamino acids, polyamides, polyalkylcyanoacrylates, and polyphosphazenes. A mixture of polymers may be used to tailor either the release characteristics of BAS in the biodegradable delivery system, or the degradation characteristics of the biodegradable delivery system or both. See column 5, lines 55-67. The reference teaches the blending of two different biodegradable polymers with varying crystallinity and amorphous states to tailor release characteristics of the delivery system. See column 4, lines 25-35.column 9, lines 30-35, and examples. The method of mixing the polymer, solvent, and drug are taught in examples. Note that NMP has a miscibility of a miscibility in water of 7% or less as defined by instant specification.

Although, Shukla teaches the blending of polymers according to their properties to manipulate release rate, Shukla et al do not exemplify the use of a polymer blend consisting of an amorphous polymer and crystalline polymer. Shukla exemplifies an amorphous polymer.

Lundgren discloses a bioresorbable material and an article of manufacture made of such material for medical use to be implanted into a living organism. See column 1, lines 5-10. Lundgren et al disclose the need for implant articles to have both dimension stability (mechanical strength) to retain the shape of the implant during the healing process and malleability so that the material can take the shape of the location it is contained within. See column 1, lines 15-50. Therefore, Lundgren et al disclose a bioresorbable material that comprises at least one amorphous polymer or copolymer selected from the group consisting of poly-d,l-lactide, and copolymers of poly-d,l-lactide and polycaprolactone, poly-l-lactide, or polytrimethylene and at least one crystalline polymer selected from the group consisting of poly-l-lactide, polycaprolactone and polydioxanone; and a plasticizer (solvent). The composition is a vehicle for the delivery of active agents. See column 5, lines 40-50. Lundgren also discloses that a small amount of crystalline polymers to amorphous polymers drastically reduces swelling of the material. Lundgren discloses that swelling has a negative influence since it forces increased pressure on the tissue and impairs mechanical strength of the implant. See column 7, lines 20-55.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Shukla et al and Lundgren and add a biodegradable crystalline polymer. One would have been motivated to do so since Lundgren teaches the criticality of having malleability and mechanical strength in an injectable implant. Further, Lundgren teaches adding crystalline polymers to amorphous polymers reduce swelling of the

implant, thus increasing mechanical strength of the implant. Therefore, one would have been motivated to add a crystalline polymer to Shukla's implant composition to provide mechanical strength to the implant once it is inserted in the body and reduce swelling of the material in the body.

Moreover, one would have been motivated to look to Lundgren's specific teaching that the instant polymer blend provides for an appropriate malleability and mechanical strength and apply it to Shukla's broad teaching of varying the properties, such as crystallinity and amorphous states, of the biodegradable polymers.

Claims 1-19, 34, 38, and 48-59 are rejected under 35 U.S.C. 103(a) as being unpatentable over US patent 6,130,200 to Brodbeck et al in view of US patent 5,525,646 to Lundgren et al.

Brodbeck et al disclose an injectable gel composition containing a biocompatible polymer(s), ethyl or benzyl benzoate, a biocompatible component solvent, a bioactive agent, and an emulsifier. See column 7, lines 25-35 (Note Examples, Tables 1-2) Brodbeck teaches biodegradable polymers include polylactides, polyglycolides, polyanhydrides, polydioxanones, polycaprolactone, PVP, etc. and mixtures thereof. See column 10, lines 65-68. Brodbeck teach a solvent having a solubility in water of less than 7% allows for suitable burst control and sustained release of the beneficial agent. The invention is directed to a method of systemically or locally administering a beneficial agent to a subject by implanting the gel into the subject.

Although Brodbeck teaches mixtures of biodegradable polymers, the reference exemplifies an amorphous polymer and does not specifically teach the instant polymer blend of an amorphous polymer with a crystalline polymer.

Lundgren discloses a bioresorbable material and an article of manufacture made of such material for medical use to be implanted into a living organism. See column 1, lines 5-10. Lundgren et al disclose the need for implant articles to have both dimension stability (mechanical strength) to retain the shape of the implant during the healing process and malleability so that the material can take the shape of the location it is contained within. See column 1, lines 15-50. Therefore, Lundgren et al disclose a bioresorbable material that comprises at least one amorphous polymer or copolymer selected from the group consisting of poly-d,l-lactide, and copolymers of poly-d,l-lactide and polycaprolactone, poly-l-lactide, or polytrimethylene and at least one crystalline polymer selected from the group consisting of poly-l-lactide, polycaprolactone and polydioxanone; and a plasticizer (solvent). The composition is a vehicle for the delivery of active agents. See column 5, lines 40-50. Lundgren also discloses that a small amount of crystalline polymers to amorphous polymers drastically reduces swelling of the material. Lundgren discloses that swelling has a negative influence since it forces increased pressure on the tissue and impairs mechanical strength of the implant. See column 7, lines 20-55.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to combine the teachings of Brodbeck et al and Lundgren and add a biodegradable crystalline polymer. One would have been motivated to do so since Lundgren teaches the criticality of having malleability and mechanical strength in a injectable implant. Further, Lundgren teaches adding crystalline polymers to amorphous polymers reduces swelling of the implant, thus increasing mechanical strength of the implant. Therefore, one would have been motivated to add a crystalline polymer to Brodbeck's implant composition to provide mechanical

strength to the implant once it is inserted in the body and reduce swelling of the material in the body.

Art of Interest

The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. US patent 5,522,895 is relied upon to demonstrate the conventional use of a crystallizable polymer and an amorphous polymer. US '895 teaches a biodegradable implant containing PLLA (crystalline polymer) and PGA (an amorphous polymer).

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharmila S. Gollamudi whose telephone number is 571-272-0614. The examiner can normally be reached on M-F (8:00-5:30), alternate Fridays off.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz can be reached on 571-272-0887. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Sharmila S. Gollamudi
Examiner
Art Unit 1616

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